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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,042	03/07/2007	Sudhanshu Vrati	U 016379-3	7944

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LADAS & PARRY LLP
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
10/02/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

nyuspatactions@ladas.com

Office Action Summary	Application No.	Applicant(s)	
	10/585,042	VRATI, SUDHANSHU	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-49* is/are pending in the application.

4a) Of the above claim(s) *21-23 and 34-49* is/are withdrawn from consideration.

5)☒ Claim(s) *33* is/are allowed.

6)☒ Claim(s) *24-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/30/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received 10/29/2008 and 5/22/2009.

Election/Restrictions

Applicant's election of group II, claims 24-33 is acknowledged. Claims 21-23 and 34-49 are withdrawn because the claims are drawn to the non-elected invention.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 24-33 are under examination in this Office Action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 30, 2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims recite "A recombinant adenovirus (RAdEs) vaccine (ECACC Accession Number 04121701)" The claims provide partial biological deposit information by reciting ECACC Accession Number 04121701. However there is no mention about the deposit of recombinant adenovirus (RAdEs) in the specification.

The specification does not provide the Biological Deposit information with regard to the recombinant adenovirus (RAdEs). The information with regard to the pAdEs plasmid of SEQ ID NO: 1 is not sufficient to provide enablement for the claimed A recombinant adenovirus (RAdEs). The claims are rejected ecause the specification does not provide adequate enablement for the claimed A recombinant adenovirus (RAdEs).

It is noted that claim 33 is not rejected because the claim and the present specification provide a sequence encoding the plasmid pAdEs, thus there is sufficient enablement for the pAdEs plasmid.

It is apparent that the recombinant adenovirus (RAdEs) is required to practice the claimed invention because they are a necessary limitation for the success of the invention as stated in the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the recombinant adenovirus (RAdEs). See 37 CFR 1.802. Therefore, access to the recombinant adenovirus (RAdEs) is required to practice the invention. The specification does not provide a repeatable method for the recombinant adenovirus (RAdEs) without access to the the recombinant adenovirus (RAdEs) and it does not appear to be readily available material.

Deposit of the recombinant adenovirus (RAdEs) in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112., because the strains would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Claims 24-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an **immunogenic composition** comprising the recombinant adenovirus RAdEs, does not reasonably provide enablement for the recombinant adenovirus RAdEs **vaccine**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, the factors deemed relevant are those of the amount of direction and the working examples provided, that

quantity of experimentation necessary, the (un)predictability of the art, and the breadth of the claims.

Claims are drawn to the recombinant adenovirus RAdEs vaccine. The phrase "vaccine" implies protection from infection with a pathogen. While Applicant's specification shows that protection of mice against Japanese encephalitis virus can be achieved by immunization with the claimed recombinant adenovirus RAdEs, Applicant's specification does not provide evidence that immunization of humans with the recombinant adenovirus RAdEs provides protection against infection with the Japanese encephalitis virus. Applicant's specification discloses that the RAdEs induced high titers of JEV neutralizing antibodies and protected the immunized mice against lethal JEV challenge. The specification provides working examples where mice were immunized intramuscular (IM) and orally with RAds. Oral route of virus delivery induced low titers of anti-JEV antibodies that had only little JEV neutralizing activity. IM immunizations with both RAdEa and RAdEs resulted in high titers of anti-JEV antibodies. RAdEa induced very low titers of JEV neutralizing antibodies whereas RAdEs inoculation resulted in high titers of JEV neutralizing antibodies. Splenocytes from mice immunized IM with RAds secreted large amounts of interferon-.gamma. and moderate amounts of interleukin-5. These splenocytes also showed cytotoxic activity against JEV-infected cells. Mice immunized IM with RAdEs showed complete protection against the lethal dose of JEV given intra-cerebral (Example 10-14). FIG. 4 shows Antibody response in mice. BALB/c mice were immunized with RAdEa, RAdEs or with the vaccine by IM or oral route of inoculation.

Applicant contemplates that the claimed recombinant adenovirus RAdE would provide protection against the infection with the Japanese encephalitis virus against in humans. The art

teaches that the vaccine against Japanese encephalitis does currently exist however the existing vaccine is a whole virus vaccine, while the claimed vaccine which is based on the recombinant adenovirus. Despite numerous studies showing protection in animals against various viruses induced by immunization with adenoviral vectors carrying viral antigens such as HIV, HCV, HBV and other viruses, a protective adenoviral based vaccine against HIV, HCV, HBV or other viruses does not currently exist (see Tatsis, Molecular Therapy, Volume 10, 2004).

In order to establish that the claimed recombinant adenovirus RAdE can provide protection against the Japanese encephalitis in humans, the skilled artisan would be required to conduct undue experimentation.

In conclusion, undue experimentation would be required to practice the claimed invention commensurate with the scope of the claims. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in specification, and the breadth of the claims, it would take undue trials and errors to practice the full scope of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaur et al. (Journal of Infectious Diseases, 2001, p. 1-12 in IDS of 6/30/2008) in view of Jaiswal et al. (Journal of Virology, December 2003, p. 12907-12913 in IDS of 6/30/2008).

Applicant's specification discloses that the recombinant adenovirus (RAdEs) of the present invention comprises the cDNA encoding the JEV E secretory protein (Es) incorporated into a replication incompetent (ΔE1/ΔE3) human adenovirus type 5 (Ad5) genome –RAd (Example 2). Thus RAd and Es is assembled to form a RAdEs). The product by process limitations in claims 24 and 32 and the intended use of the claimed vaccine recited in claims 26-31 are not considered limiting.

Kaur et al. teach the cDNA encoding the JEV E secretory protein and immunization of mice using plasmids encoding the JEV E secretory protein (see Materials and Methods). Jaiswal et al. teach replication incompetent (ΔE1/ΔE3) human adenovirus type 5 (Ad5) genome expressing the ectodomain of the Dengue Virus Type 2 envelope protein and generation of immune responses due to administration of the chimeric adenoviral vector in mice (see the entire document). It would have been obvious to incorporate Kaur's cDNA encoding JEV E secretory

protein into Jaiswal's replication incompetent (ΔE1/ΔE3) human adenovirus type 5 (Ad5) genome, because Kaur teaches that immune responses generated against JEV E secretory protein resulted in 60% protection against challenged animals and because Jaiswal et al. teach that his adenovirus vector (RAd) effectively induces immune responses against chimeric antigens (see page 12907).

The present claims would have been obvious because the **substitution** of one known element Dengue Virus Type 2 envelope protein, taught by Jaiswal for another JEV E secretory protein, taught by Kaur would have yielded predictable results to one of ordinary skill in the art at the time of the invention, i.e adenoviral vector expressing the JEV E secretory protein –RadEs. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

SEQ ID NO: 1 is free of prior art of record. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-

8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached at 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/
Examiner, Art Unit 1648